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| FULL ESTIMATED COST | 0.21 | 0.21 |

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FILE 'SCISEARCH' ENTERED AT 11:56:42 ON 28 SEP 2002


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FILE 'WELDASEARCH' ENTERED AT 11:56:42 ON 28 SEP 2002


FILE 'WSCA' ENTERED AT 11:56:42 ON 28 SEP 2002


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=> polysaccharide
=> s polysaccharide
  40 FILES SEARCHED...
L1      239378 POLYSACCHARIDE

=> s li and glycosaminoglycan
  39 FILES SEARCHED...
L2          40 LI AND GLYCOSAMINOGLYCAN

=> s l2 and K5
L3           1 L2 AND K5

=> dis l3 bib abs

L3   ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2002 ISI (R)
AN   97:816986  SCISEARCH
GA   The Genuine Article (R) Number: YD473
TI   Biosynthesis of heparin/heparan sulfate - DNA cloning and expression of
     D-glucuronyl C5-epimerase from bovine lung
AU   Li J P (Reprint); HagnerMcWhirter A; Kjellen L; Palgi J; Jalkanen M;
     Lindahl U
CS   UNIV UPPSALA, DEPT MED & PHYSIOL CHEM, POB 575, S-75123 UPPSALA, SWEDEN
     (Reprint); SWEDISH UNIV AGR SCI, CTR BIOMED, DEPT VET MED CHEM, S-75123
     UPPSALA, SWEDEN; UNIV TURKU, CTR BIOTECHNOL, FIN-20520 TURKU, FINLAND; ABO
     AKAD UNIV, FIN-20520 TURKU, FINLAND
CYA  SWEDEN; FINLAND
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (31 OCT 1997) Vol. 272, No. 44, pp.
     28158-28163.
     Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE
```

PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 33
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Glucuronyl C5-epimerases catalyze the conversion of D-glucuronic acid (GlcUA) to L-iduronic acid (IdceA) units during the biosynthesis of **glycosaminoglycans**. An epimerase implicated in the generation of heparin/heparan sulfate was previously purified to homogeneity from bovine liver (Campbell, P., Hannesson, H. H., Sandback, D., Roden, L., Lindahl, U., and **Li**, J.-p, (1994) J. Biol. Chem. 269, 2695-26958). The present report describes the molecular cloning and functional expression of the lung enzyme, The cloned enzyme contains 444 amino acid residues and has a molecular mass of 49,905 Da, N-terminal sequence analysis of the isolated liver enzyme showed this species to be a truncated form lacking a 73-residue N-terminal domain of the deduced amino acid sequence.
The coding cDNA insert was cloned into a baculovirus expression vector and expressed in Sf9 insect cells, Cells infected with recombinant epimerase showed a 20-30-fold increase in enzyme activity, measured as release of (H2O)-H-3 from a polysaccharide substrate containing C5-H-3-labeled hexuronic acid units. Furthermore, incubation of the expressed protein with the appropriate (GlcUA-GlcNSO(3))(n) substrate resulted in conversion of similar to 20% of the GlcUA units into IdceA residues, Northern analysis implicated two epimerase transcripts in both bovine lung and liver tissues, a dominant similar to 9-kilobase (kb) mRNA and a minor similar to 5-kb species, Mouse mastocytoma cells showed only the similar to 5-kb transcript. A comparison of the cloned epimerase with the enzymes catalyzing an analogous reaction in alginate biosynthesis revealed no apparent amino acid sequence similarity.

```
=> s l1 and K5
  42 FILES SEARCHED...
L4          351 L1 AND K5

=> s l4 and epimer?
L5           33 L4 AND EPIMER?

=> s l5 and enzyme
  36 FILES SEARCHED...
L6           20 L5 AND ENZYME

=> s l6 and immobil?
  37 FILES SEARCHED...
L7            5 L6 AND IMMOBIL?

=> dis l7 1-5 bib abs

L7    ANSWER 1 OF 5  BIOTECHNO  COPYRIGHT 2002 Elsevier Science B.V.
AN    1994:24332896   BIOTECHNO
TI    Biosynthesis of heparin/heparan sulfate. Purification of the D-glucuronyl
      C-5 epimerase from bovine liver
AU    Campbell P.; Hannesson H.H.; Sandback D.; Roden L.; Lindahl U.; Li J.-P.
CS    Dept. of Medical/Physiological Chem., Biomedical Center, University of
      Uppsala,S-751 23 Uppsala, Sweden.
SO    Journal of Biological Chemistry, (1994), 269/43 (26953-26958)
      CODEN: JBCHA3  ISSN: 0021-9258
DT    Journal; Article
CY    United States
LA    English
SL    English
AB    The D-glucuronyl C-5 epimerase involved in the biosynthesis of
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heparin/heparan sulfate was purified from the high speed supernatant fraction of a homogenate of bovine liver by chromatography on **immobilized** O-desulfated heparin, red Sepharose, phenyl Sepharose, and concanavalin A-Sepharose. After close to 1 million-fold purification, in 10-15% yield, the product gave a single band on SDS-polyacrylamide gel electrophoresis with silver staining and had a mobility corresponding to an M(r) of .sim.52,000. Since the **epimerase** assay used in the course of purification was based on release of tritium, as .cents..sup.3H!H.sub.2O, from a .cents.5-.sup.3H!uronyl-labeled substrate, it was important to establish that the purified **enzyme** did indeed catalyze the actual conversion of D-glucuronyl to L-iduronyl residues. Upon incubation of the purified **enzyme** with .sup.3H-labeled heparosan N-sulfate, prepared by metabolic labeling (with D-.cents.1-.sup.3H!glucose) of a capsular **polysaccharide** from Escherichia coli **K5** and subsequent chemical partial N-deacetylation and N-sulfation, approximately 30% of the D-glucuronyl residues located between two N-sulfated glucosamine units were converted to L-iduronyl units.

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2002:392262 CAPLUS
DN 136:380105
TI Glycosaminoglycans derived from **k5 polysaccharide** having high anticoagulant and antithrombotic activities and process for their preparation
IN Oreste, Pasqua; Zoppetti, Giorgio
PA Italy
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 738,879.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002062019 | A1 | 20020523 | US 2001-950003 | 20010912 |
| | IT 2000MI0665 | A1 | 20011001 | IT 2000-MI665 | 20000330 |
| | WO 2002050125 | A2 | 20020627 | WO 2001-IB2492 | 20011217 |
| | WO 2002050125 | A3 | 20020822 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | |
|---|---|---|---|
| PRAI | IT 2000-MI665 | A | 20000330 |
| | US 2000-738879 | A2 | 20001218 |
| | US 2001-950003 | A | 20010912 |

AB Glycosaminoglycans derived from **K5 polysaccharide** having high anticoagulant and antithrombotic activity and useful for the control of coagulation and as antithrombotic agents are obtained starting from an optionally purified **K5 polysaccharide** by a process comprising the steps of N-deacetylation/N-sulfation, C5 **epimerization**, O-oversulfation, selective O-desulfation, 6-O-sulfation, N-sulfation, and optional depolymn., in which said **epimerization** is performed with the use of the **enzyme** glucoronosyl C5 **epimerase** in soln. or in **immobilized** form in the presence of divalent cations. New, particularly interesting antithrombin compds. are obtained by controlling the reaction time in the selective O-desulfation step and submitting the product obtained at the end of the final N-sulfation step to depolymerization.

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 2001:730838 CAPLUS
DN 135:267246
TI Glycosaminoglycans derived from the **k5 polysaccharide** having high anticoagulant and antithrombotic activity and process for their preparation
IN Zoppetti, Giorgio; Oreste, Pasqua; Cipolletti, Giovanni
PA Inalco S.p.A., Italy
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001072848 | A1 | 20011004 | WO 2001-EP3461 | 20010327 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| IT 2000MI0665 | A1 | 20011001 | IT 2000-MI665 | 20000330 |
| PRAI IT 2000-MI665 | A | 20000330 | | |

AB Glycosaminoglycans derived from the **K5 polysaccharide** having high anticoagulant and antithrombotic activity obtained by a process comprising the prepn. of the **K5 polysaccharide** from Escherichia coli, N-deacetylation/N-sulfation, C-5 **epimerization**, supersulfation, selective O-desulfation, selective 6-O sulfation and N-sulfation, wherein said **epimerization** is carried out using the glucuronosyl C-5 **epimerase enzyme** in soln. or in **immobilized** form in presence of specific divalent cations.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
AN 1994:624763 CAPLUS
DN 121:224763
TI Biosynthesis of heparin/heparan sulfate. Purification of the D-glucuronyl C-5 **epimerase** from bovine liver
AU Campbell, Patrick; Hannesoson, Helgi H.; Sandbaeck, Dagmar; Roden, Lennart; Lindahl, Ulf; Li, Jin-ping
CS Univ. Alabama, Birmingham, AL, 35294, USA
SO Journal of Biological Chemistry (1994), 269(43), 26953-8
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The D-glucuronyl C-5 **epimerase** involved in the biosynthesis of heparin/heparan sulfate was purified from the high speed supernatant fraction of a homogenate of bovine liver by chromatog. on **immobilized** O-desulfate heparin, red Sepharose, Ph Sepharose, and Con A-Sepharose. After close to 1 million-fold purifn., 10-15% yield, the product gave a single band on SDS-PAGE with silver staining and had a mobility corresponding to an Mr of .apprx.52,000. Since the **epimerase** assay used in the course of purifn. was based on release of tritium, as [3H]H2O, from a [5-3H]uronyl-labeled substrate, it was important to establish that the purified **enzyme** did indeed catalyze the actual conversion of D-glucuronyl to L-iduronyl residues. Upon incubation of the purified **enzyme** with 3H-labeled heparosan

N-sulfate, prepd. by metabolic labeling (with D-[1-3H]glucose) of a capsular **polysaccharide** from Escherichia coli **K5** and subsequent chem. partial N-deacetylation and N-sulfation, approx. 30% of the D-glucuronyl residues located between two N-sulfated glucosamine units were converted to L-iduronyl units.

L7 ANSWER 5 OF 5 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 94:733790 SCISEARCH
GA The Genuine Article (R) Number: PQ931
TI BIOSYNTHESIS OF HEPARIN/HEPARAN SULFATE - PURIFICATION OF THE D-GLUCURONYL C-5 **EPIMERASE** FROM BOVINE LIVER
AU CAMPBELL P; HANNESSON H H; SANDBACK D; RODEN L; LINDAHL U; LI J P (Reprint)
CS UNIV UPPSALA, DEPT MED & PHYSIOL CHEM, BOX 575, S-75123 UPPSALA, SWEDEN (Reprint); UNIV UPPSALA, DEPT MED & PHYSIOL CHEM, S-75123 UPPSALA, SWEDEN; UNIV ALABAMA, BIRMINGHAM, AL, 35294
CYA SWEDEN; USA
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (28 OCT 1994) Vol. 269, No. 43, pp. 26953-26958.
ISSN: 0021-9258.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 21
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB The D-glucuronyl C-5 **epimerase** involved in the biosynthesis of heparin/heparan sulfate was purified from the high speed supernatant fraction of a homogenate of bovine liver by chromatography on **immobilized** O-desulfated heparin, red Sepharose, phenyl Sepharose, and concanavalin A-Sepharose. After close to 1 million-fold purification, in 10-15% yield, the product gave a single band on SDS-polyacrylamide gel electrophoresis with silver staining and had a mobility corresponding to an M(r) of similar to 52,000. Since the **epimerase** assay used in the course of purification was based on release of tritium, as [H-3]H2O, from a [5-H-3]uronyl-labeled substrate, it was important to establish that the purified **enzyme** did indeed catalyze the actual conversion of D-glucuronyl to L-iduronyl residues. Upon incubation of the purified **enzyme** with H-3-labeled heparosan N-sulfate, prepared by metabolic labeling (with D-[1-H-3]glucose) of a capsular **polysaccharide** from Escherichia coli **K5** and subsequent chemical partial N-deacetylation and N-sulfation, approximately 30% of the D-glucuronyl residues located between two N-sulfated glucosamine units were converted to L-iduronyl units.

=> dis hist

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FILE 'AGRICOLA, ALUMINIUM, ANABSTR, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, DKILIT, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 11:56:42 ON 28 SEP 2002

L1 239378 S POLYSACCHARIDE
L2 40 S LI AND GLYCOSAMINOGLYCAN
L3 1 S L2 AND K5
L4 351 S L1 AND K5
L5 33 S L4 AND EPIMER?
L6 20 S L5 AND ENZYME
L7 5 S L6 AND IMMOBIL?

=> s l2 and composition
35 FILES SEARCHED...

L8 1 L2 AND COMPOSITION

=> dis l8 bib abs

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2002:532818 CAPLUS
TI Extracellular matrix **composition** of full-thickness defect repair tissue is little influenced by exercise in rat articular cartilage
AU Espanha, M. Margarida; Lammi, Pirkko E.; Hyttinen, Mika M.; Lammi, Mikko J.; Helminen, Heikki J.
CS Faculty of Human Kinetics, Technical University of Lisboa, Lisbon, Port.
SO Connective Tissue Research (2001), 42(2), 97-109
CODEN: CVTRBC; ISSN: 0300-8207
PB Gordon & Breach Science Publishers
DT Journal
LA English
AB Full-thickness articular cartilage defects in the femoral condyles of adult rats were examd. four and eight weeks after injury. Quant. polarized light microscopic anal. showed that birefringence of the tissue in the central repair area increased more in rats exercised on a treadmill. **Glycosaminoglycan** content in the repair tissue was also higher than in the intermittent active motion group at four weeks after injury, but by eight weeks the levels were similar in both groups. No normal-looking articular cartilage was formed in the lesions, and only in one animal type **lI** collagen was obsd. in the superficial zone of repair tissue. No 3B3(-) antigenicity of the proteoglycans was seen during repair. In conclusion, exercise minimally modified the repair of full-thickness articular cartilage defects in adult rats. The repair in the exercised group may occur slightly faster in the early stages but no difference was seen at the eight week time interval between the exercised and the intermittently active group.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis hist

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FILE 'AGRICOLA, ALUMINIUM, ANABSTR, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, DKILIT, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 11:56:42 ON 28 SEP 2002
L1 239378 S POLYSACCHARIDE
L2 40 S LI AND GLYCOSAMINOGLYCAN
L3 1 S L2 AND K5
L4 351 S L1 AND K5
L5 33 S L4 AND EPIMER?
L6 20 S L5 AND ENZYME
L7 5 S L6 AND IMMOBIL?
L8 1 S L2 AND COMPOSITION

=> s l4 and composition
39 FILES SEARCHED...
L9 13 L4 AND COMPOSITION

=> s l9 and glycosaminoglycan
42 FILES SEARCHED...
L10 0 L9 AND GLYCOSAMINOGLYCAN

=> s l9 and carrier
39 FILES SEARCHED...
L11 0 L9 AND CARRIER

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=> s l9 and ion?
  20 FILES SEARCHED...
  36 FILES SEARCHED...
L12          1 L9 AND ION?

=> dis l12 bib abs

L12  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   1984:2544  CAPLUS
DN   100:2544
TI   Assay of N-acetylheparosan deacetylase with a capsular
     polysaccharide from Escherichia coli K5 as substrate
AU   Navia, Juan Luis; Riesenfeld, Johan; Vann, Willie F.; Lindahl, Ulf; Roden,
     Lennart
CS   Inst. Dent. Res., Univ. Alabama, Birmingham, AL, 35294, USA
SO   Anal. Biochem. (1983), 135(1), 134-40
     CODEN: ANBCA2; ISSN: 0003-2697
DT   Journal
LA   English
AB   A new substrate for N-acetylheparosan deacetylase was prepd.  The capsular
     polysaccharide from E. coli 010:K5:H4, which is
     structurally identical to N-acetylheparosan, was partially N-deacetylated
     by hydrazinolysis and was then radioactively labeled by N-acetylation with
     [3H]acetic anhydride.  Upon incubation of the labeled
     polysaccharide with microsomes from the Furth mastocytoma,
     [3H]acetyl groups were released, demonstrating that the bacterial
     polysaccharide was a substrate for the N-deacetylase.  Reaction
     conditions were established which permitted the quant. assay of
     N-deacetylase activity; a Km of 74 mg polysaccharide/L was detd.
     which corresponds to 2.1 .times. 10-4M, expressed as concn. of uronic
     acid; the Vmax was 3.4 nmol/mg protein/L.  In confirmation of previous
     results, it was obsd. (1) that the reaction was stimulated by
     3'-phosphoadenylylsulfate (up to a max. of 45% at a concn. of 0.5 mM),
     suggesting that N-sulfation occurred which facilitated continued action of
     the N-deacetylase, and (2) that NaCl and KCl inhibited the enzyme, with
     50% redn. of activity at a concn. of 25 mM.  In the course of this work, a
     simple, single-vial assay procedure was used.  Released [3H]acetate was
     extd. from the acidified reaction mixt. with a toluene- or xylene-based
     scintillation fluid contg. 10% isoamyl alc. and measured directly by
     scintillation spectrometry.


=> s glycosaminoglycans
L13      23302 GLYCOSAMINOGLYCANS

=> s l13 and K5
L14          47 L13 AND K5

=> s l14 and process
  25 FILES SEARCHED...
L15          7 L14 AND PROCESS

=> s l15 deacetyla?
MISSING OPERATOR L15 DEACETYLA?
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l15 and deacetyla?
L16          6 L15 AND DEACETYLA?

=> s l16 and N-sulfat?
 75% OF LIMIT FOR L#S REACHED
  26 FILES SEARCHED...
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L17 6 L16 AND N-SULFAT?

=> dis l17 1-6 bib abs

L17 ANSWER 1 OF 6 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
AN 2001:32989368 BIOTECHNO
TI Toward a biotechnological heparin through combined chemical and enzymatic modification of the Escherichia coli **K5** polysaccharide
AU Naggi A.; Torri G.; Casu B.; Oreste P.; Zoppetti G.; Li J.P.; Lindahl U.
CS Prof. B. Casu, G. Ronzoni Research Institute, via G. Colombo, 81-20133 Milano, Italy.
E-mail: casu@ronzoni.it
SO Seminars in Thrombosis and Hemostasis, (2001), 27/5 (437-443), 26 reference(s)
CODEN: STHMBV ISSN: 0094-6176
DT Journal; General Review
CY United States
LA English
SL English
AB A **process** to generate **glycosaminoglycans** with heparin- and heparan sulfate-like sequences from the Escherichia coli **K5** capsular polysaccharide is described. This polymer has the same structure as N-acetylheparosan, the precursor in heparin/heparan sulfate biosynthesis. The **process** involves chemical N-**deacetylation** and **N-sulfation**, enzymatic conversion of up to 60% of the D-glucuronic acid to L-iduronic acid residues, and chemical O-sulfation. Because direct sulfation afforded unwanted 3-O-sulfated (instead of 2-O-sulfated) iduronic acid residues, a strategy involving graded solvolytic desulfation of chemically oversulfated C5-epimerized sulfaminoheparosans was assessed using persulfated heparin and heparan sulfate as model compounds. The O-desulfation **process** was shown to increase the anti-factor Xa activity of oversulfated heparin.

L17 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2002:392262 CAPLUS
DN 136:380105
TI **Glycosaminoglycans** derived from **k5** polysaccharide having high anticoagulant and antithrombotic activities and **process** for their preparation
IN Oreste, Pasqua; Zoppetti, Giorgio
PA Italy
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 738,879.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002062019 | A1 | 20020523 | US 2001-950003 | 20010912 |
| | IT 2000MI0665 | A1 | 20011001 | IT 2000-MI665 | 20000330 |
| | WO 2002050125 | A2 | 20020627 | WO 2001-IB2492 | 20011217 |
| | WO 2002050125 | A3 | 20020822 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IT 2000-MI665 A 20000330

US 2000-738879 A2 20001218
US 2001-950003 A 20010912

AB **Glycosaminoglycans** derived from **K5** polysaccharide having high anticoagulant and antithrombotic activity and useful for the control of coagulation and as antithrombotic agents are obtained starting from an optionally purified **K5** polysaccharide by a **process** comprising the steps of N-**deacetylation**/**N-sulfation**, C5 epimerization, O-oversulfation, selective O-desulfation, 6-O-sulfation, **N-sulfation**, and optional depolymn., in which said epimerization is performed with the use of the enzyme glucoronosyl C5 epimerase in soln. or in immobilized form in the presence of divalent cations. New, particularly interesting antithrombin compds. are obtained by controlling the reaction time in the selective O-desulfation step and submitting the product obtained at the end of the final **N-sulfation** step to depolymerizazion.

L17 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2001:840398 CAPLUS
DN 136:167613
TI Toward a biotechnological heparin through combined chemical and enzymatic modification of the Escherichia coli **K5** polysaccharide
AU Naggi, Annamaria; Torri, Giangiacomo; Casu, Benito; Oreste, Pasqua; Zoppetti, Giorgio; Li, Jin-Ping; Lindahl, Ulf
CS G. Ronzoni Institute for Chemical and Biochemical Research, Milan, Italy
SO Seminars in Thrombosis and Hemostasis (2001), 27(5), 437-443
CODEN: STHMBV; ISSN: 0094-6176
PB Thieme Medical Publishers, Inc.
DT Journal
LA English

AB A **process** to generate **glycosaminoglycans** with heparin and heparan sulfate-like sequences from the Escherichia coli **K5** capsular polysaccharide is described. This polymer has the same structure as N-acetylheparosan, the precursor in heparin/heparan sulfate biosynthesis. The **process** involves chem. N-**deacetylation** and **N-sulfation**, enzymic conversion of up to 60% of the D-glucuronic acid to L-iduronic acid residues, and chem. O-sulfation. Because direct sulfation afforded unwanted 3-O-sulfated (instead of 2-O-sulfated) iduronic acid residues, a strategy involving graded solvolytic desulfation of chem. over-sulfated C5-epimerized sulfaminoheparosans was assessed using persulfated heparin and heparan sulfate as model compds. The O-desulfation **process** was shown to increase the anti-factor Xa activity of over-sulfated heparin.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2001:730838 CAPLUS
DN 135:267246
TI **Glycosaminoglycans** derived from the **k5** polysaccharide having high anticoagulant and antithrombotic activity and **process** for their preparation
IN Zoppetti, Giorgio; Oreste, Pasqua; Cipolletti, Giovanni
PA Inalco S.p.A., Italy
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001072848 | A1 | 20011004 | WO 2001-EP3461 | 20010327 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

IT 2000MI0665 A1 20011001 IT 2000-MI665 20000330
PRAI IT 2000-MI665 A 20000330

AB **Glycosaminoglycans** derived from the **K5** polysaccharide having high anticoagulant and antithrombotic activity obtained by a **process** comprising the prepn. of the **K5** polysaccharide from Escherichia coli, N-**deacetylation/N-sulfation**, C-5 epimerization, supersulfation, selective O-desulfation, selective 6-O sulfation and **N-sulfation**, wherein said epimerization is carried out using the glucuronosyl C-5 epimerase enzyme in soln. or in immobilized form in presence of specific divalent cations.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 6 PASCAL COPYRIGHT 2002 INIST-CNRS. ALL RIGHTS RESERVED.
AN 2002-0168335 PASCAL
CP Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TIEN Toward a biotechnological heparin through combined chemical and enzymatic modification of the Escherichia coli **K5** polysaccharide Glycoaminoglycans
AU NAGGI Annamaria; TORRI Giangiacomo; CASU Benito; ORESTE Pasqua; ZOPPETTI Giorgio; LI Jin-Ping; LINDAHL Ulf
HARENBERG Job (ed.)
CS G. Ronzoni Institute for Chemical and Biochemical Research, Milan, Italy; Inalco, Montale, Pistoia, Italy; Department of Medical Biochemical Microbiology, University of Uppsala, Uppsala, Sweden
SO Seminars in thrombosis and hemostasis, (2001), 27(5), 437-443, 26 refs.
ISSN: 0094-6176 CODEN: STHMBV
DT Journal
BL Analytic
CY United States
LA English
AV INIST-17786, 354000094741730010
CP Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
AB A **process** to generate **glycosaminoglycans** with heparin- and heparan sulfate-like sequences from the Escherichia coli **K5** capsular polysaccharide is described. This polymer has the same structure as N-acetylheparosan, the precursor in heparin/ heparan sulfate biosynthesis. The **process** involves chemical N-**deacetylation** and **N-sulfation**, enzymatic conversion of up to 60% of the D-glucuronic acid to L-iduronic acid residues, and chemical O-sulfation. Because direct sulfation afforded unwanted 3-O-sulfated (instead of 2-O-sulfated) iduronic acid residues, a strategy involving graded solvolytic desulfation of chemically oversulfated C5-epimerized sulfaminoheparosans was assessed using persulfated heparin and heparan sulfate as model compounds. The O-desulfation **process** was shown to increase the anti-factor Xa activity of oversulfated heparin.

L17 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 2001:876964 SCISEARCH
GA The Genuine Article (R) Number: 486YG
TI Toward a biotechnological heparin through combined chemical and enzymatic modification of the Escherichia coli **K5** polysaccharide
AU Naggi A; Torri G; Casu B (Reprint); Oreste P; Zoppetti G; Li J P; Lindahl U
CS G Ronzoni Res Inst, Via G Colombo, 81, I-20133 Milan, Italy (Reprint); G

Ronzoni Res Inst, I-20133 Milan, Italy; G Ronzoni Inst Chem & Biochem Res, Milan, Italy; Inalco, Montale, Pistoia, Italy; Univ Uppsala, Dept Med Biochem Microbiol, S-75105 Uppsala, Sweden
CYA Italy; Sweden
SO SEMINARS IN THROMBOSIS AND HEMOSTASIS, (OCT 2001) Vol. 27, No. 5, pp. 437-443.
Publisher: THIEME MEDICAL PUBL INC, 333 SEVENTH AVE, NEW YORK, NY 10001 USA.
ISSN: 0094-6176.
DT Article; Journal
LA English
REC Reference Count: 26
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB A **process** to generate **glycosaminoglycans** with heparin- and heparan sulfate-like sequences from the Escherichia coli **K5** capsular polysaccharide is described. This polymer has the same structure as N-acetylheparosan, the precursor in heparin/ heparan sulfate biosynthesis. The **process** involves chemical N-**deacetylation** and **N-sulfation**, enzymatic conversion of up to 60% of the D-glucuronic acid to L-iduronic acid residues, and chemical O-sulfation. Because direct sulfation afforded unwanted 3-O-sulfated (instead of 2-O-sulfated) iduronic acid residues, a strategy involving graded solvolytic desulfation of chemically oversulfated C5-epimerized sulfaminoheparosans was assessed using persulfated heparin and heparan sulfate as model compounds. The O-desulfation **process** was shown to increase the anti-factor Xa activity of oversulfated heparin.